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**Original Article**

# Clinical Effectiveness of Benzoyl Peroxide and Clindamycin Combination Therapy in the Treatment of Papulopustular Acne

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## ABSTRACT

Acne is a prevalent inflammatory skin condition affecting 9% of the global population. Its impact on quality of life and self-esteem leads to depression and anxiety. Combination regimen may be effective in treating acne. **Objective:** To assess the clinical effectiveness of a fixed-dose combination of 1% clindamycin and 5% benzoyl peroxide in the treatment of mild to moderate papulopustular acne. **Methods:** An observational prospective study was conducted from June 2023 to December 2023 in the dermatology department of Niazi Welfare Foundation Teaching Hospital, Sargodha. 72 patients with mild to moderate papulopustular acne were monitored. A gel containing a combination of 1% clindamycin and 5% benzoyl peroxide was applied once daily for 12 weeks. Descriptive statistics was used for demographic variables. Chi-square test was used to evaluate the treatment effects at a significance level, p-value<0.05. Adverse effects related to therapy were shown as bar chart. **Results:** Findings of the study showed that during therapy in the period between the 3rd and 6th weeks, the proportion of patients who achieved excellent improvement increased by 25% from 40/72 (55.5%) to 57/72 (79.1%) respectively p < 0.05. **Conclusions:** The study concluded that the combination of 1% clindamycin and 5% benzoyl peroxide was effective in treating mild to moderate papulopustular acne.

## INTRODUCTION

Acne is a prevalent inflammatory skin condition affecting 9% of the global population [1]. Acne manifest frequently during puberty, between the ages of 12 and 24. The incidence of acne increased among individuals aged 25 to 40 [3, 4]. Acne's impact on quality of life and self-esteem is notably significant, often leading to feelings of depression and anxiety [2, 3]. The pathogenetic links that play a significant role in the development of acne are well known; hypertrophy of the sebaceous glands and excessive formation of sebum, abnormal keratinization of keratinocytes in the area of the mouths of hair follicles, follicular proliferation of *Cutibacterium acnes (C. acnes),* development of inflammation [4, 5]. Modern methods of studying *C. acnes*, based on typing the nucleic acids of microorganisms, have made it possible to establish that this bacterium, which is one of the dominant representatives of the normal microbiome of human skin, consists of phylogenetically different cluster groups [6]. Different phylotypes of *C. acnes* differ significantly in their characteristics, including the ability to initiate inflammation in the skin [7]. If in healthy people *C. acnes* are commensals involved in maintaining the barrier properties of the skin, then in patients with acne other phylotypes of this bacterium act as opportunistic microorganisms and

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are the main triggers of inflammation [8, 9]. In acne, *C. acnes* strains stimulate the production of interleukin-1α by keratinocytes, which leads to their infundibular hyperproliferation and the formation of comedones [10, 11]. A systematic review of scientific articles on the epidemiology of acne revealed that severe cases requiring systemic therapy occur in fewer than 10% of patients for 90% of patients with mild to moderate acne, treatment typically starts with the application of topical medications [12]. Combining pharmacological drug with varying mechanisms of action in a single external dosage form compared with therapy with a single-component agent or sequential use of two topical drugs can provide higher effectiveness and tolerability, reduce antibiotic resistance and increase patient adherence to treatment [13, 14]. Clindamycin belongs to lincosamide antibiotic group and had a bacteriostatic effect against gram-positive aerobic microorganisms as well as a broad spectrum of anaerobic bacteria. Topical clindamycin has proven highly effective in treating papulopustular acne; however, prolonged monotherapy can result in antibiotic resistance in *C. acnes* and lead to disease relapses [15]. Benzoyl peroxide is a highly lipophilic oxidizing agent with bactericidal and mild keratolytic effects. Its nonspecific bactericidal action occurs through the formation of reactive oxygen species that oxidize bacterial proteins. Using benzoyl peroxide helps decrease comedone formation and prevents microorganisms from developing resistance to clindamycin [16].

The current study aimed to assess the effectiveness of a combination drug containing a fixed dose of 1% clindamycin and 5% benzoyl peroxide in treating patients with mild to moderate papulopustular acne.

## METHODS

An observational prospective study was carried out from June 2023 to December 2023 in the dermatology department of Niazi Welfare Foundation Teaching Hospital, Sargodha approved by the Institutional Review Board with the letter reference number NM&DC/IRB/407. IRB approval was granted on 1st June 2023. The sample size of 72 patients was calculated based on a 95% confidence level, a 5% margin of error, and the prevalence of acne reported in recent studies in Pakistan [17]. Non-probability convenience sampling was employed. Inclusion criteria involved patients aged over 12 years, with mild to moderate non-papulopustular acne, who were able to adhere to the protocol requirements. Patients with severe papulopustular acne, nodular or conglobate acne, a history of antibiotic-associated colitis, hypersensitivity to clindamycin or lincomycin, pregnancy, breastfeeding, or liver and kidney failure were excluded. Data collection commenced after obtaining the informed consent from participants. Demographic information, including sex, age was collected and, the disease severity assessed according to half-face counting [18]. The subjects were categorized according to following severity scale. Only cases with mild to moderate severity were included: 1) fewer than 10 comedones, 2) between 10 and 25 comedones, 3) between 25 and 50 comedones 4) more than 50 comedones. Before baseline measurements of physiological parameters, it was ensured that the skin area to be measured is clean and free of any cosmetics or lotions. The room was acclimatized to a standard temperature (20-22°C). Sebum on one cheek was determined with Sebummeter SM815 (Courage + Khazaka Electronic GmbH, Germany). The measuring head of the cartridge exposes a 64 mm2 measuring section of an opaque plastic tape which is firmly pressed onto the cheeks for 30s with a slight pressure to collect the sebum. The resulting increase in transparency of the tape was measured and the displayed values correspond to the sebum amount on the face in µg sebum/cm2. Procedure for using the gel was explained to the participants that was to be applied once daily as a thin layer to the area of the rash for period of 3 months. The effect of treatment was assessed at 3rd and 6th week of treatment by examining counts of rashes on half of the face along with measures of physiological parameters. Effectiveness of therapy was based on the reduction in lesions. All the measures were taken at baseline, 3 weeks and 6 week period. Patients were also monitored for adverse events. Main outcome variable of the study was effectiveness of therapy evaluated on scale of acne severity based on percentage of reduction in comedones on half face after 3 weeks of treatment and again after 6 weeks [18]. Statistical data processing was carried out using the software SPSS version 24.0. The normality of distributions was checked using the Shapiro–Wilk test. Descriptive statistics was used for demographic variables. Chi-square test was used to evaluate the treatment effects at a significance level, p-value<0.05. Adverse effects related to therapy were shown as bar chart.

**Table 1:** Scale of Acne Severity

| Scale | Percentage of Reduction | Level |
|---|---|---|
| 4 | 100% Reduction | Excellent |
| 3 | 75–99% Reduction | Good |
| 2 | 50–74% Reduction | Moderate |
| 1 | 1–49% Reduction | Insufficient |
| 0 | 0% Reduction | Unchanged |
| -1 | Increase in Severity | Worse |

## RESULTS

There were 72 patients, including both men and women aged 14 to 35 years (mean age 20.9 ± 5.7 years), diagnosed with mild to moderate papulopustular acne. Among them, there were 40 men (55.6%, mean age 21.4 ± 4.8 years) and 32 women (44.4%, mean age 19.6 ± 6.5 years). 31 patients (43%) had mild papulopustular acne, while 41 (57%) had

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moderate severity as shown in table 2.

**Table 2:** Demographics of Study Participant (n=72)

| Variables | No. of Participants Range/ (Mean ± SD)/N (%) |
|---|---|
| Age (Years) | 14-35 |
| Mean Age (Years) | 20.9 ± 5.7 |
| **Gender** | |
| Male | 40 (55.6%) |
| Female | 32 (44.4%) |
| **Disease Severity** | |
| Fewer than 10 Comedones | 31 (43%) |
| Between 10 and 25 Comedones | 41 (57%) |

Table 3 showed that by the end of the 3rd week, over half of the patients had achieved excellent improvement 40 out of 72 (55.5%); improvement was good in 22 out of 72 (30.5%) patients; moderate improvement in 7 out of 72 (10%); and there was insufficient improvement in 3 out of 72 (4.1%) patients. The total proportion of patients who experienced excellent and good improvement was 62 out of 72 (86%). By the end of the 6th week of treatment, 79.1% (57 out of 72) of patients had achieved excellent improvement. The total proportion of patients showing excellent and good improvement was 88.8% (64 out of 72), while insufficient improvement was observed in 2.7% (2 out of 72) of patients. Analysis of the dynamics of the clinical picture showed that during therapy in the period between the 3rd and 6th weeks, the proportion of patients who achieved excellent improvement increased by 25% from 40/72 (55.5%) to 57/72 (79.1%) respectively $p < 0.05$.

**Table 3:** The Clinical Effectiveness of Therapy

| Outcomes | Effectiveness of Therapy N (%) | | p-Value |
|---|---|---|---|
| | 3 Weeks | 6 Weeks | |
| Excellent | 40 (55.6%) | 57 (79.1%) | 0.01 |
| Good | 22 (30.6%) | 7 (9.72%) | |
| Moderate | 7 (9.7%) | 6 (8.3%) | |
| Insufficient | 3 (4.2%) | 2 (2.8%) | |
| Unchanged | 0 | 0 | |
| Worse | 0 | 0 | |

During the treatment, some patients experienced side effects such as dry skin (13%, 9 out of 72), redness (20%, 14 out of 72), and a burning sensation after applying the medication (13%, 9 out of 72). These side effects were temporary and resolved without the need for additional prescriptions. No adverse reactions necessitating discontinuation of the medication were reported throughout the study period as shown in figure 1.

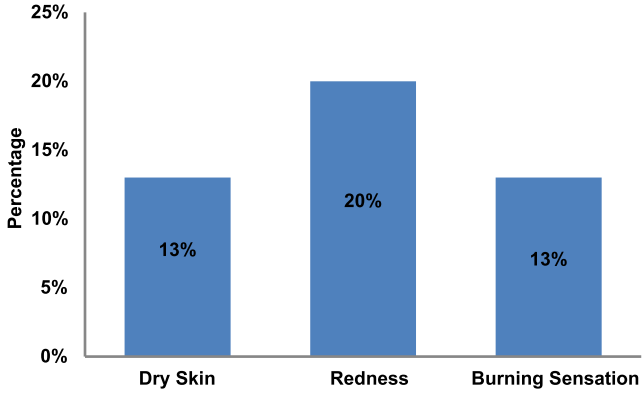


**Figure 1:** Adverse Effects Reported During the Study

## DISCUSSION

This study focuses on evaluating the therapeutic effectiveness and tolerability of a new combination topical medication for acne a gel containing a fixed dose of 1% clindamycin and 5% benzoyl peroxide. The results indicate the high clinical effectiveness. According to findings in table 2, by the end of the 6th week of treatment, 79.1% (57 out of 72) of patients had achieved excellent improvement while it was only 55.5% (40 out of 72) in 3rd week. Another study evaluating the effectiveness of a gel formulation combining benzoyl peroxide and clindamycin demonstrated significantly greater reductions in both inflammatory and total lesions. There were no serious adverse events requiring discontinuation of treatment. The combination gel was generally well tolerated, with only a few patients experiencing short-term adverse events after application of the drug. These findings suggest that the combination therapy is more effective than its individual components [19]. Another study reported that the combination therapy of adapalene and benzoyl peroxide demonstrated a success rate of 89.2%, defined as maintaining the number of inflammatory lesions at ≤10. These findings suggest that the combination treatment regimen is significantly more effective than no treatment in managing inflammatory lesions [20]. Similarly, Mohsin N *et al.*, in 2022 study also indicated the significant effectiveness of combination therapy using benzoyl peroxide and clindamycin for acne treatment, as it offers superior effectiveness in improving acne and reducing both inflammatory and total lesions [21]. The combination of 1% clindamycin and 5% benzoyl peroxide proved significant in improving acne, with notable results in 6 weeks therapy. However, as an observational study, emphasizing the need for experimental studies with controls to investigate the effectiveness of combination regimen further. Future clinical trials are needed to evaluate the effectiveness of dual therapies for more definite results.

## CONCLUSIONS

The study concluded that the combination of 1% clindamycin and 5% benzoyl peroxide was effective in treating mild to moderate papulopustular acne.

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Combination regime proved effective and well tolerated than individual ingredient alone.

## Authors Contribution

Conceptualization: SN
Methodology: SN, SM, ZP
Formal analysis: AG
Writing, review and editing: MAH, SA, ZP

All authors have read and agreed to the published version of the manuscript.

## Conflicts of Interest

The authors declare no conflict of interest.

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